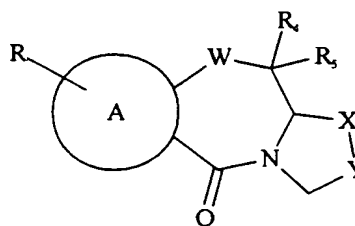
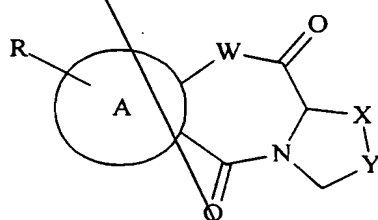


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We claim:

1. A method of inhibiting a HIV integrase, the method comprising:  
 exposing the integrase to an integrase inhibiting amount of one or more  
 anti-integrase compounds selected from the group consisting of the following  
 5 compounds, or pharmaceutically acceptable salts thereof:



wherein

A is thiazole, benzene, naphthalene, pyridine, pyrimidine, pyrazine, or quinoline;

R is one or more of H, halogen, lower alkyl, lower alkoxy, NO<sub>2</sub>, lower ester or carboxylic acid;

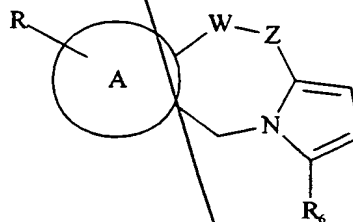
X-Y is CH<sub>2</sub>-S, S-CH<sub>2</sub>, CH<sub>2</sub>-O, CH<sub>2</sub>-S(O), S(O)-CH<sub>2</sub>, CH<sub>2</sub>-CH<sub>2</sub>, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>, or CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>;

R<sub>4</sub> is H or hydroxy;

R<sub>5</sub> is H, phenyl, or alkylamine; and

W is S or O.

or wherein the compound is



wherein

A is thiazole, benzene, naphthalene, pyridine, pyrimidine, pyrazine, or quinoline; and

R is one or more of H, halogen, lower alkyl, lower ester or carboxylic acid;

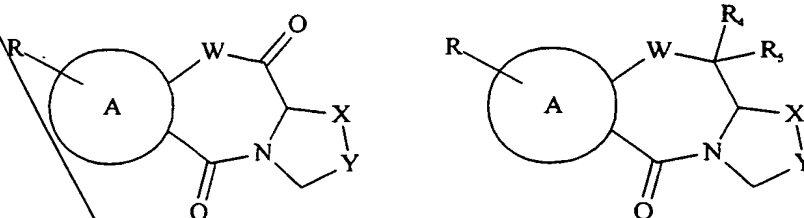
R<sub>6</sub> is H, substituted or unsubstituted alkyl or amine;

W is S or O; and

Z is S, O, CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, or C=O.

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2. The method of claim 1, wherein the compound is selected from the group consisting of:



wherein X-Y is CH<sub>2</sub>-S, S-CH<sub>2</sub>, CH<sub>2</sub>-O, or CH<sub>2</sub>-CH<sub>2</sub>, and W is S.

3. The method of claim 2, wherein:

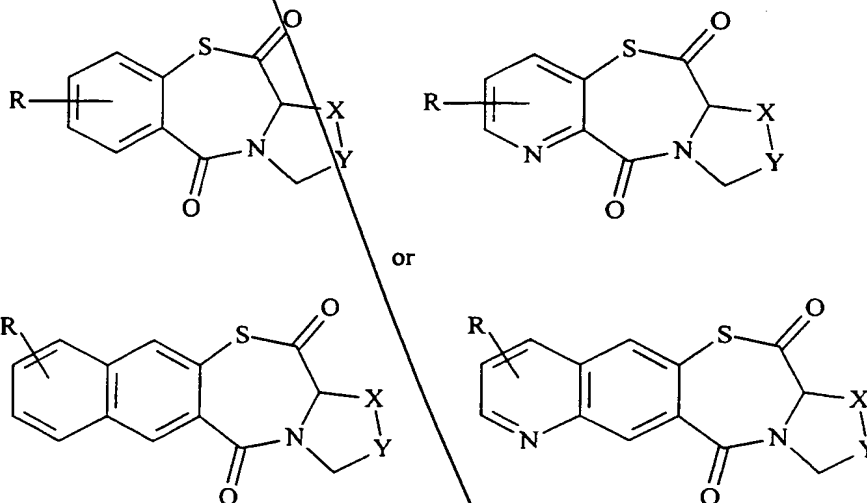
A is benzene, naphthalene, pyridine, pyrimidine, pyrazine, or quinoline.

4. The method of claim 3, wherein A is benzene or naphthalene.

5. The method of claim 4, wherein R is H, halogen, lower alkoxy, or

NO<sub>2</sub>.

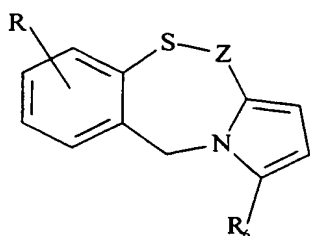
6. The method of claim 1, wherein the compound is:



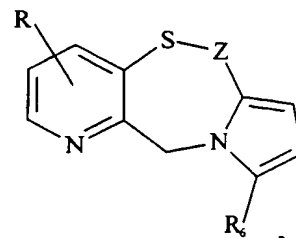
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- 40 -

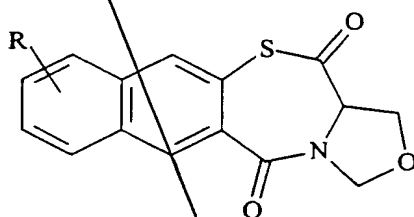
7. The method of claim 1, wherein the compound is:



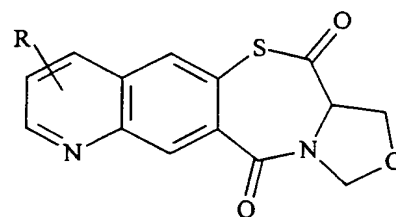
or



8. The method of claim 6, wherein the compound is

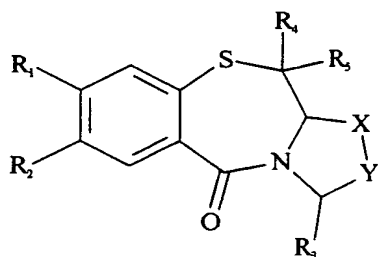
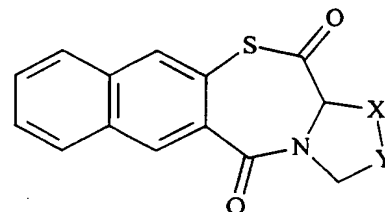
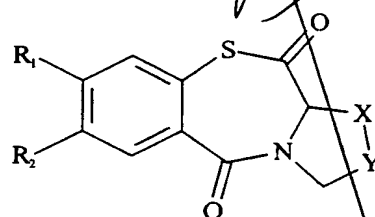


or

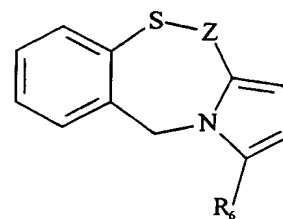


- 5 9. following:

The method of claim 1, wherein the compound is one of the



or



wherein X-Y is S-CH<sub>2</sub>, CH<sub>2</sub>-S, CH<sub>2</sub>-O, CH<sub>2</sub>-CH<sub>2</sub>, S(O)-CH<sub>2</sub>, or CH<sub>2</sub>-S(O);

R<sub>1</sub> and R<sub>2</sub> are independently selected from the group consisting of H, NO<sub>2</sub>,

10 halogen, lower alkyl or lower alkoxy;

R<sub>3</sub> is H or phenyl;

R<sub>4</sub> is H or hydroxy;

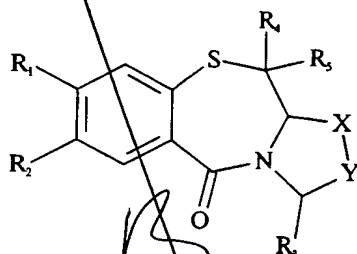
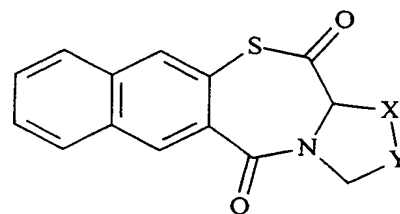
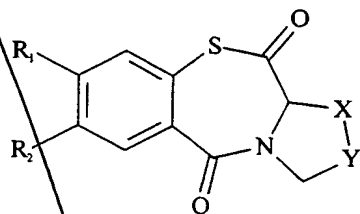
R<sub>5</sub> is H, phenyl or alkylamine; and

- 41 -

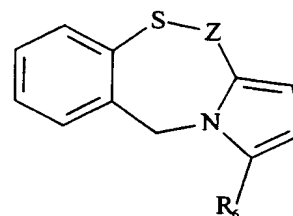
$R_6$  is H, phenyl or alkylamine.

10. The method of claim 9, wherein the alkylamine is  $-N(CH_2CH_2)_2NCH_3$ ,  $-CH_2NCH_2CH_3$ , or  $-CH_2N(CH_2CH_2)_2NCH_3$ .

11. The method of claim 7, wherein the compound is



or



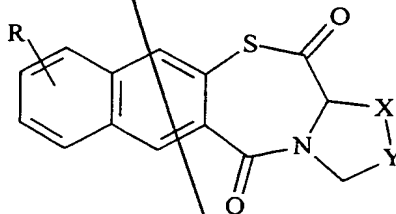
X-Y is  $S-CH_2$ ,  $CH_2-S$ , or  $CH_2-S(O)$ ;

10 and  $R_1$  and  $R_2$  are independently selected from the group consisting of H,  $NO_2$ , halogen, lower alkyl and lower alkoxy;

$R_3$  is H; and

$R_4$ ,  $R_5$ , and  $R_6$  are H.

12. The method of claim 1, wherein the compound is



15 and X-Y is  $S-CH_2$  or  $CH_2-S$ .

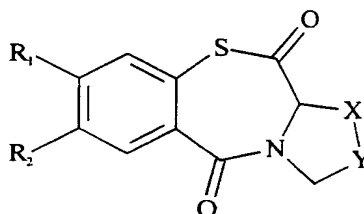
13. The method of claim 12, wherein R is H.

14. The method of claim 13, wherein X-Y is  $S-CH_2$ .

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15. The method of claim 9, wherein  
R<sub>1</sub> is H, NO<sub>2</sub>, or lower alkoxy,  
R<sub>2</sub> is H, Cl, Br, lower alkyl, or lower alkoxy;  
R<sub>3</sub> and R<sub>4</sub> are H;  
R<sub>5</sub> is N(CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>3</sub>; and  
X-Y is CH<sub>2</sub>-S, S-CH<sub>2</sub>, or CH<sub>2</sub>-CH<sub>2</sub>.

16. The method of claim 15 wherein the compound is



- wherein R<sub>1</sub> is H, NO<sub>2</sub>, or methoxy;  
R<sub>2</sub> is H, halogen or methoxy; and  
X-Y is CH<sub>2</sub>-S or S-CH<sub>2</sub>.

17. The method of claim 1, wherein the compound is administered in a therapeutically effective amount to a subject.

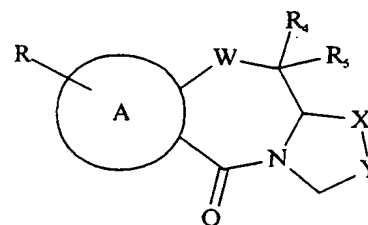
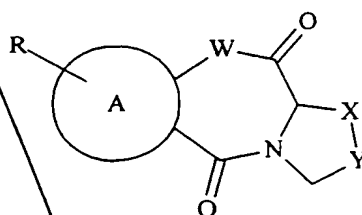
18. The method of claim 17, wherein the method is a method of treating or preventing HIV infection in the subject.

19. The method of claim 15, wherein the compound is administered in a therapeutically effective amount to a subject to treat or prevent an HIV infection.

20. The method of claim 16, wherein the compound is administered in a therapeutically effective amount to a subject to treat or prevent an HIV infection.

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21. A method of treating or preventing HIV infection in a subject, comprising administering to the subject a therapeutically effective amount of a compound selected from the group consisting of:



wherein

5 A is thiazole, benzene, naphthalene, pyridine, pyrimidine, pyrazine, or quinoline;

R is one or more of H, halogen, lower alkyl, lower alkoxy, NO<sub>2</sub>, lower ester or carboxylic acid;

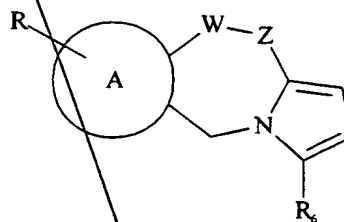
10 X-Y is CH<sub>2</sub>-S, S-CH<sub>2</sub>, CH<sub>2</sub>-O, CH<sub>2</sub>-S(O), S(O)-CH<sub>2</sub>, CH<sub>2</sub>-CH<sub>2</sub>, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>, or CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>;

R<sub>4</sub> is H or hydroxy;

R<sub>5</sub> is H, phenyl, or alkylamine; and

W is S or O.

15 or wherein the compound is



wherein

A is thiazole, benzene, naphthalene, pyridine, pyrimidine, pyrazine, or quinoline; and

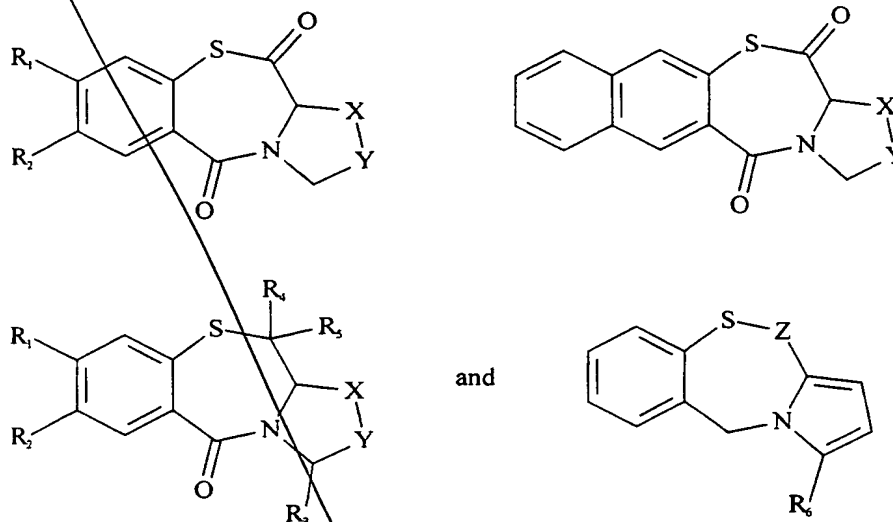
20 R is selected from the group of H, halogen, lower alkyl, lower ester or carboxylic acid;

R<sub>6</sub> is H, substituted or unsubstituted alkyl or amine;

W is S or O; and

Z is S, O, CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, or C=O.

22. The method of claim 21, wherein the compound is selected from the group consisting of:



wherein X-Y is S-CH<sub>2</sub>, CH<sub>2</sub>-S, CH<sub>2</sub>CH<sub>2</sub> or S(O)CH<sub>2</sub>;

R<sub>1</sub> is H, NO<sub>2</sub>, or lower alkoxy;

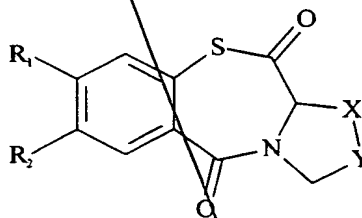
R<sub>2</sub> is H, Cl, Br, lower alkyl, or lower alkoxy;

R<sub>3</sub> and R<sub>4</sub> are H;

R<sub>5</sub> is N(CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>3</sub>; and

R<sub>6</sub> is H.

23. The method of claim 21, wherein the compound is



and

R<sub>1</sub> and R<sub>2</sub> are H, and X-Y is S-CH<sub>2</sub>; or

R<sub>1</sub> is H, R<sub>2</sub> is Cl or Br or methyl, and X-Y is S-CH<sub>2</sub>; or

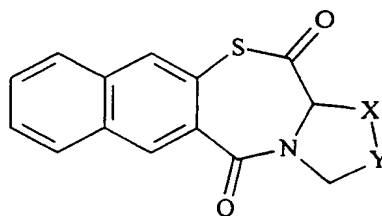
R<sub>1</sub> is NO<sub>2</sub>, R<sub>2</sub> is H, and X-Y is CH<sub>2</sub>-S; or

R<sub>1</sub> and R<sub>2</sub> are methoxy, and X-Y is CH<sub>2</sub>-S; or

R<sub>1</sub> is H, R<sub>2</sub> is methyl, and X-Y is S(O)-CH<sub>2</sub>.

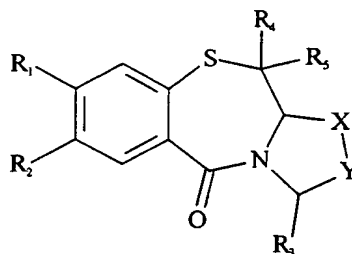
- 45 -

24. The method of claim 21, wherein the compound is



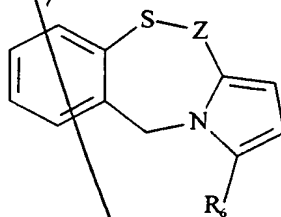
wherein X-Y is S-CH<sub>2</sub> or CH<sub>2</sub>-S.

25. The method of claim 21, wherein the compound is



wherein X-Y is CH<sub>2</sub>-CH<sub>2</sub>;  
R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are H; and  
R<sub>5</sub> is N(CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>3</sub>.

26. The method of claim 21, wherein the compound comprises



wherein R<sub>6</sub> is H and Z is C=O.

27. The method of claim 1, wherein  
A is thiazole, benzene, naphthalene, pyridine, pyrimidine, pyrazine, or  
quinoline;

R is one or more of halogen or NO<sub>2</sub>;

X-Y is CH<sub>2</sub>-S, S-CH<sub>2</sub>, CH<sub>2</sub>-O, CH<sub>2</sub>-S(O), S(O)-CH<sub>2</sub>, CH<sub>2</sub>-CH<sub>2</sub>, CH<sub>2</sub>-CH<sub>2</sub>-  
CH<sub>2</sub>, or CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>;

R<sub>4</sub> is H or hydroxy;

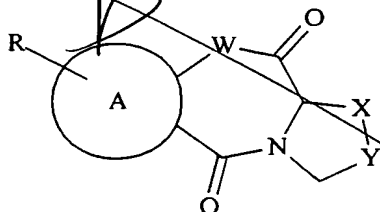
R<sub>5</sub> is H, phenyl, or alkylamine;



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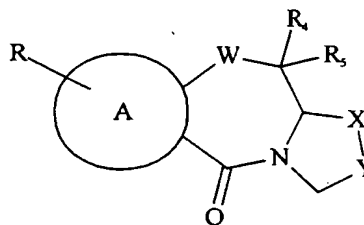
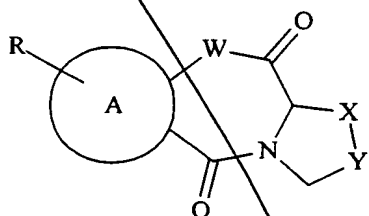
$R_6$  is H, or substituted or unsubstituted alkyl or amine; and  
W is S or O.

28. The method of claim 21, wherein the compound comprises



5 and A is benzene or naphthalene;  
R is H,  $\text{NO}_2$ , or lower alkoxy; and  
X-Y is  $\text{CH}_2\text{-S}$  or  $\text{S-CH}_2$ .

10 29. A compound having the following formula, or a pharmaceutically acceptable salt thereof:



wherein A is thiazole, benzene, naphthalene, pyridine, pyrimidine, pyrazine, or quinoline;

R is one or more of halogen or  $\text{NO}_2$ ;

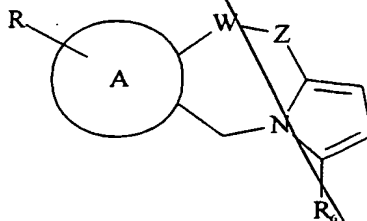
X-Y is  $\text{CH}_2\text{-S}$ ,  $\text{S-CH}_2$ ,  $\text{CH}_2\text{-O}$ ,  $\text{CH}_2\text{-S(O)}$ ,  $\text{S(O)-CH}_2$ ,  $\text{CH}_2\text{-CH}_2$ ,  $\text{CH}_2\text{-CH}_2\text{-CH}_2$ , or  $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2$ ;

$R_4$  is H or hydroxy;

$R_5$  is H, phenyl, or alkylamine; and

W is S or O.

20 or wherein the compound is



wherein

Sub  
B1

A is thiazole, benzene, naphthalene, pyridine, pyrimidine, pyrazine, or quinoline; and

R is one or more of halogen or NO<sub>2</sub>;

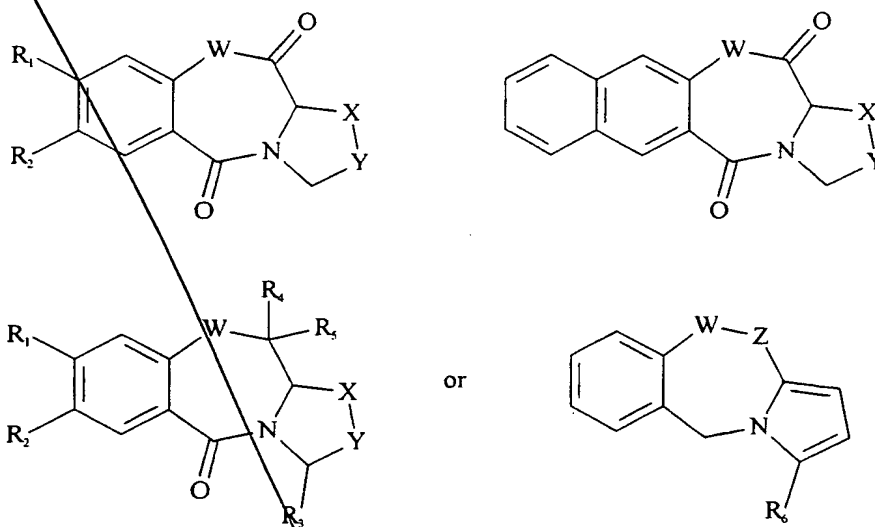
R<sub>6</sub> is H, substituted or unsubstituted alkyl or amine;

W is S or O; and

Z is S, O, CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, or C=O.

5

30. A compound having the following formula, or a pharmaceutically acceptable salt thereof, wherein the compound is:



10

wherein

X-Y is S-CH<sub>2</sub>, CH<sub>2</sub>-S, S(O)-CH<sub>2</sub>, CH<sub>2</sub>-S(O), or CH<sub>2</sub>CH<sub>2</sub>;

W is S or O;

R<sub>1</sub> is H or NO<sub>2</sub>;

R<sub>2</sub> is H, halogen, lower alkyl or lower alkoxy;

15

R<sub>3</sub> is H;

R<sub>4</sub> is hydroxy or H;

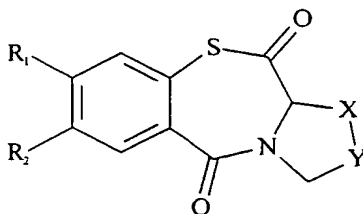
R<sub>5</sub> is phenyl or N(CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>3</sub>; and

R<sub>6</sub> is CH<sub>2</sub>N(CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>3</sub>,

provided that R<sub>1</sub> and R<sub>2</sub> are not both H or not both alkoxy.

20

31. The compound of claim 30, wherein the compound is



and  $R_1$  is H or  $\text{NO}_2$ ;

R<sub>2</sub> is H, halogen, lower alkyl or lower alkoxy;

provided that R<sub>1</sub> and R<sub>2</sub> are not both H or not both alkoxy.

5 32. The compound of claim 30, wherein

$R_1$  is H,  $R_2$  is ~~Cl~~, X-Y is S-CH<sub>2</sub>; or

$R_1$  is H,  $R_2$  is Br, X-Y is S-CH<sub>2</sub>; or

$R_1$  is H,  $R_2$  is  $CH_3$ , X-Y is S- $CH_2$ ; or

$R_1$  is H,  $R_2$  is H,  $X-Y$  is  $CH_2-S$ ; or

10  $R_1$  is H,  $R_2$  is Cl,  $X-Y$  is  $CH_2-S$ ; or

$R_1$  is H,  $R_2$  is Br, X-Y is  $\text{CH}_2\text{-S}$ ; or

$R_1$  is H,  $R_2$  is  $CH_3$ ,  $X-Y$  is  $CH_2-S$ ; or

$R_1$  is  $\text{NO}_2$ ,  $R_2$  is H,  $X-Y$  is  $\text{CH}_2\text{-S}$ ; or

$R_1$  is H,  $R_2$  is  $OCH_3$ ,  $X-Y$  is  $CH_2-S$ ; or

15 R<sub>1</sub> is H, R<sub>2</sub> is H, X-Y is ~~CH<sub>2</sub>-O~~; or

$R_1$  is H,  $R_2$  is  $CH_3$ , X-Y is  $S(O)-CH_2$ ; or

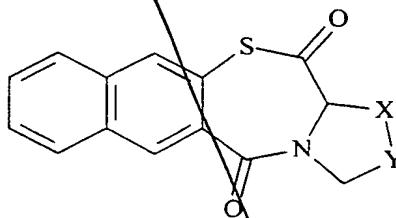
$R_1$  is H,  $R_2$  is H, X-Y is  $\text{CH}_2\text{-S(O)}$ ; or

$R_1$  is H,  $R_2$  is Cl, X-Y is  $\text{CH}_2\text{-S(O)}$ ; or

$R_1$  is H,  $R_2$  is  $OCH_3$ , X-Y is  $CH_2-S(O)$ .

20

33. The compound of claim 30, wherein the compound is

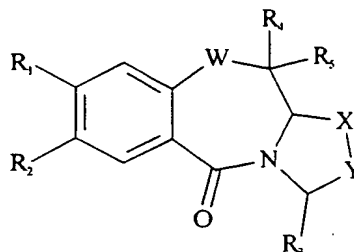
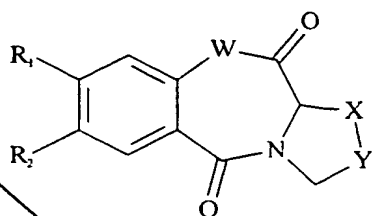


and X-Y is S-CH<sub>2</sub> or CH<sub>2</sub>-S.

34. The compound of claim 30, wherein X-Y is S-CH<sub>2</sub>.

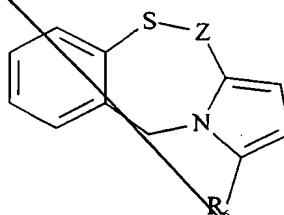
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35. The compound of claim 30, wherein the compound is:



and  $R_1$ ,  $R_2$  and  $R_3$  are H,  $R_4$  is OH or H;  
 $R_5$  is Ph or  $N(CH_2CH_2)_2CH_3$ ; and  
 $X-Y$  is  $CH_2-CH_2$ .

- 5      36. The compound of claim 30, wherein the compound is



and  $R_6$  is  $CH_2N(CH_2CH_2)_2NCH_3$ .

- 10      37. A pharmaceutical composition comprising the compound of claim 29, or the pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier.

- 15      38. A pharmaceutical composition comprising the compound of claim 30, or the pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier.

- 20      39. A method of screening for an anti-HIV integrase drug, comprising:  
 providing an assay of HIV integrase inhibition; and  
 using the assay to screen for drugs comprising analogs or derivatives of  
 any of the compounds of claim 1.

40. The method of claim 39, wherein the assay detects a thiazepine compound that inhibits human immunodeficiency virus type-1 integrase (HIV-1 IN).

- 50 -

41. The method of claim 40, further comprising detecting a thiazepine having no detectable effect on reverse transcriptase, protease, and virus attachment.
- 5 42. The method of claim 39, wherein the compound is a thiazolothiazepine.
43. The compound of claim 29, for use in a pharmaceutical composition for the inhibition of HIV integrase.
- 10 44. The compound of claim 43, for use in the treatment of HIV infection.
- 15 45. The compound of claim 44, for use as a prophylactic treatment against HIV infection.
- 

add  
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